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EXAMINER	
ZHOU, SHUBO	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	10/086,748	WOLBER ET AL.	
	Examiner	Art Unit	
	Shubo "Joe" Zhou	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-14 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-14 is/are rejected.

7)☒ Claim(s) 9 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 11 June 2002 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/22/02, 5/19/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Sequence Rules Compliance

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because of the following:

(1) Although such sequences as those appeared in Table 8 on pages 28-30 of the specification are each assigned a sequence identifier (SEQ ID NO:X), the paper copy and computer readable form (CRF) of a Sequence Listing, and a statement under 37 CFR 1.821(f) are not provided in the application;

(2) The nucleic acid sequence on page 35 of the specification is not followed by a sequence identifier. Applicants are reminded that it is required that SEQ ID Nos be amended into the specification at each sequence that is encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2).

A paper copy and CRF of a Sequence Listing that includes all sequences disclosed in the application that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), as well as a statement under 37 CFR 1.821(f), are required. Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to comply with these requirements may result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be

obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

Information Disclosure Statement

2. The Information Disclosure Statement filed 8/22/02 has been entered and considered. Initialed copy of the form PTO-1449 is enclosed with this action. As to the IDS filed 5/19/03, based on the copies of the documents provided to the Office by applicants, errors appear to be present in the listing of two documents on the PTO-1449: WO 95/10365 should be WO 97/10365, and WO 00/26512 should be WO 00/26412. Please note that the examiner has corrected the listings and considered the documents.

3. The citations/listings of publications and/or patents or websites in various sections of the specification such as those on pages 29 and 33, etc. are not a proper Information Disclosure Statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

4. The specification is objected to because of the following:

5. The U.S. Application number 09/322,692 disclosed on page 29 of the specification is now U.S. Patent No. 6,132,997. Applicant is requested to update the specification with the U.S.

Patent number. Applicant is also requested to update the status of U.S. Application number 09/659,173 disclosed on page 1 as now abandoned.

6. The disclosure is objected to also because it contains an embedded hyperlink and/or other form or browser-executable code. Such code is present in the specification at page 33. Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP ' 608.01.

7. Appropriate correction is required.

Claim Objections, Warning

8. Applicant is advised that should claim 8 be found allowable, claim 9 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case, the difference between the two claims is that claim 8 requires calculating the average signal intensity from calibrating probes, whereas claim 9 requires calculating the mean signal intensity from calibrating probes. Absent a specific definition for each of the terms, average and mean, they are considered to be the same in the context of the claims (mean: the average value of a set of numbers. Dictionary.com http://dictionary.reference.com/search?q=mean).

Claim Rejections-35 USC § 112

9. The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-9 are rejected under 35 U.S.C. 112 , second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "the set of calibration features" in claim 1, line 12, and in the dependent claims of claim 1, lacks clear antecedent basis. No calibrating features are recited earlier. It is not clear whether it refers to the previously recited "set of calibrating probes", and/or other calibrating features.

Claim Rejections-35 USC § 101

11. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claims 13 and 14 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 13 and 14, as currently written, are drawn to normalized signal intensities, which is merely a compilation or arrangement of data, which is deemed to be non-functional descriptive material and non-statutory subject matter. See MPEP 2106, (IV)(B)(1).

Claim Rejections-35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1, and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Lockhart et al. (IDS document: WO 97/10365, 3/20/1997).

The claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that hybridize to a sufficient fraction of target molecules in a sample to produce a signal intensity, and normalizing signals of features on the array using the calibrating probes by calculating a collective signal intensity. Due to lack of a specific definition for the term "collective signal intensity" in the specification, it is interpreted as total signal intensities of the calibrating probes (collective: assembled or accumulated into a whole. Dictionary.com http://dictionary.reference.com/search?q=collective).

Lockhart et al. disclose a method of using oligonucleotide array for monitoring gene expression. The method comprises using an array containing not only oligonucleotide probes referred to as "test probes", but also control probes used for calibration. The control probes include normalization controls, expression level controls such as probes from housekeeping genes, and mismatch controls. In one embodiment, Lockhart et al. teach that signals read from all other probes in the array are divided by the signals from the normalization control probes. See pages 34-35. Further, Lockhart et al. teach that the normalization of a signal can be accomplished by dividing the measured signal from the other probes in the array by the average signal produced by the normalization controls, and that normalization may also include correction for variations due to sample preparation and amplification. Such normalization may be accomplished by dividing the signal of a probe by the average signal from the sample

preparation/amplification control probes (e.g. the Bio B probes). See pages 53-54. It would have been readily recognized by one of skill in the art that when the average intensity from the control probes is calculated, a total intensity of the probes must have also been calculated. All the control probes disclosed by Lockhart et al. are interpreted as calibrating probes as in the instant claims because they are used to calibrate the signals of the test probes. The calibrating probes disclosed by Lockhart et al. will hybridize to a fraction of the target molecules in the sample solutions to which the array is exposed for hybridization because the housekeeping genes, etc. are contained in the sample solutions.

Claim Rejections-35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 1-3, 5, and 7-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (WO 97/10365, 3/20/1997), as applied to claims 1, and 7-9 above, in view of Chenchik et al. (US patent no. 6,077,673, Date of Patent: June 20, 2000) and further in view of Lewin, B., (Genes IV, 1990, Oxford University Press).

The instant claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that either hybridize to a sufficient fraction of target molecules in a sample solution to which the array is exposed for hybridization or hybridize to a majority of target molecules in the sample solution, and normalizing signals of features on the array using the calibrating probes by calculating a collective signal intensity. Claims 2-3 also require that the calibrating probes are poly(A) oligonucleotides.

As applied to claims 1, and 7-9, above, Lockhart et al. disclose a method of using oligonucleotide array for monitoring gene expression. The array is exposed to a sample solution containing cDNA molecules derived from the mRNA molecules from a biological sample. The method comprises using an array containing not only oligonucleotide probes referred to as "test

probes", but also control probes used for calibration. The control probes include normalization controls, expression level controls such as probes from housekeeping genes, and mismatch controls. In one embodiment, Lockhart et al. teach that signals read from all other probes in the array are divided by the signals from the normalization control probes. See pages 34-35. Further, Lockhart et al. teach that the normalization of a signal can be accomplished by dividing the measured signal from the other probes in the array by the average signal produced by the normalization controls, and that normalization may also include correction for variations due to sample preparation and amplification. Such normalization may be accomplished by dividing the signal of a probe by the average signal from the sample preparation/amplification control probes (e.g. the Bio B probes). See pages 53-54. It would have been readily recognized by one of skill in the art that when the average intensity from the control probes is calculated, a total intensity of the probes must have also been calculated. All the control probes disclosed by Lockhart et al. are interpreted as calibrating probes as in the instant claims because they are used to calibrate the signals of the test probes. The calibrating probes disclosed by Lockhart et al. will hybridize to a fraction of the target molecules in the sample solutions to which the array is exposed for hybridization because the housekeeping genes, etc. are contained in the sample solutions. Further, Lockhart et al. disclose a computer system to analyze the signal intensities detected from the array hybridization including computer readable medium on which data including signal intensities are stored and analyzed. See pages 55-56, and Figures 6-8.

However, Lockhart et al. do not explicitly recite that poly(A) oligonucleotides are used as calibrating probes, and that the calibrating probes hybridize to a majority of the target molecules in the sample solution to which the array is exposed.

Chenchik et al. disclose a nucleic acid microarray and a process of using same for gene expression monitoring. The array is exposed to a sample solution containing cDNA molecules derived from the mRNA from a biological sample. In addition to the "probe spots", the array also comprises "calibration spots" and "control spots" (column 4, lines 12-20). Chenchik et al. indicate that the calibrating and control spots are to "provide other useful information, such as background or basal level of expression, and the like', and such spots "serve in the normalization of mRNA abundance and standardization of hybridization signal intensity in the sample assayed with the array" (column 8, lines 50-67 and column 9). While Chenchik et al. do not explicitly disclose using poly(A) oligonucleotides as calibrating spots, they do motivate/suggest doing such by emphasizing that the calibrating probes should not be unique to a particular target in the sample, but "common" to the targets (column 8, lines 50-67).

A person of ordinary skill in the art would have been motivated by Chenchik et al. to search for probes that are common to the targets in the sample solution to modify Lockhart et al. to provide more calibrating probes for the microarray analysis.

Lewin teaches that poly(A) tail is common to eukaryotic, such as human mRNA. Since the target molecules contained in the sample solutions to which the array is exposed for hybridization in the method disclosed by Lockhart et al. are cDNAs, and since the cDNAs are derived from mRNAs by reverse transcription using oligo(dT) as primers followed by PCR amplification (Lockhart et al. page 39), it would have been obvious to one of ordinary skill in the art that oligo(dT) or poly(A) would be commonly present in the cDNA targets due to the way they are made, and on of ordinary skill in the art would have been motivated by Lewin and Chenchik et al. to modify the method of Lockhart et al. to include poly(A) oligonucleotides on

the array as extra calibrating probes. Such poly(A) oligonucleotides would hybridize to the majority of the target molecules due to the presence of poly(T) thereon. There would have been a reasonable expectation of success because Lockhart et al. and Chenchik et al. provide the details of procedures for making an array, preparing cDNA samples for hybridization, and making poly(A) oligonucleotides would have been known and routine skill in the art. Note that by poly(A) oligonucleotides it is meant that the oligonucleotides consist of, or comprise, consecutive multiple "As".

Therefore, the invention would have been obvious to a person of ordinary skill in the art at the time the invention was made.

19. Claims 1, 4, and 7-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (WO 97/10365, 3/20/1997), as applied to claims 1, and 7-9 above, in view of Chenchik et al. (US patent no. 6,077,673, Date of Patent: June 20, 2000) and further in view of Darnell et al. (Molecular Cell Biology, Eds., 1990, published by Scientific American Books).

The instant claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that either hybridize to a sufficient fraction of target molecules in a sample solution to which the array is exposed for hybridization or hybridize to a majority of target molecules in the sample solution, and normalizing signals of features on the array using the calibrating probes by calculating a collective signal intensity. Claim 4 also requires that the calibrating probes comprise Alu repeat sequences.

As applied to claims 1, and 7-9, above, Lockhart et al. disclose a method of using oligonucleotide array for monitoring gene expression. The array is exposed to a sample solution

containing cDNA molecules derived from the mRNA from a biological sample. The method comprises using an array containing not only oligonucleotide probes referred to as "test probes", but also control probes used for calibration. The control probes include normalization controls, expression level controls such as probes from housekeeping genes, and mismatch controls. In one embodiment, Lockhart et al. teach that signals read from all other probes in the array are divided by the signals from the normalization control probes. See pages 34-35. Further, Lockhart et al. teach that the normalization of a signal can be accomplished by dividing the measured signal from the other probes in the array by the average signal produced by the normalization controls, and that normalization may also include correction for variations due to sample preparation and amplification. Such normalization may be accomplished by dividing the signal of a probe by the average signal from the sample preparation/amplification control probes (e.g. the Bio B probes). See pages 53-54. It would have been readily recognized by one of skill in the art that when the average intensity from the control probes is calculated, a total intensity of the probes must have also been calculated. All the control probes disclosed by Lockhart et al. are interpreted as calibrating probes as in the instant claims because they are used to calibrate the signals of the test probes. The calibrating probes disclosed by Lockhart et al. will hybridize to a fraction of the target molecules in the sample solutions to which the array is exposed for hybridization because the housekeeping genes, etc. are contained in the sample solutions. Further, Lockhart et al. disclose a computer system to analyze the signal intensities detected from the array hybridization including computer readable medium on which data including signal intensities are stored and analyzed. See pages 55-56, and Figures 6-8.

However, Lockhart et al. do not explicitly recite that oligonucleotide comprising Alu sequences are used as calibrating probes, and that the calibrating probes hybridize to a majority of the target molecules in the sample solution to which the array is exposed.

Chenchik et al. disclose a nucleic acid microarray and a process of using same for gene expression monitoring. The array is exposed to a sample solution containing cDNA molecules derived from the mRNA from a biological sample. In addition to the "probe spots", the array also comprises "calibration spots" and "control spots" (column 4, lines 12-20). Chenchik et al. indicate that the calibrating and control spots are to "provide other useful information, such as background or basal level of expression, and the like', and such spots "serve in the normalization of mRNA abundance and standardization of hybridization signal intensity in the sample assayed with the array" (column 8, lines 50-67 and column 9). While Chenchik et al. do not explicitly disclose using Alu oligonucleotides as calibrating spots, they do motivate/suggest doing such by emphasizing that the calibrating probes should not be unique to a particular target in the sample, but "common" to the targets (column 8, lines 50-67).

A person of ordinary skill in the art would have been motivated by Chenchik et al. to search for probes that are common to the targets in the sample solution to modify Lockhart et al. to provide more calibrating probes for the microarray analysis.

Darnell et al. teach that Alu sequence is common to human genes and mRNA (see pages 373-374). It would have been obvious to one of ordinary skill in the art that such common Alu sequence would meet the requirement for a calibrating probe set by Chenchik et al. Thus, one of ordinary skill in the art would have been motivated by Chenchik et al. and Darnell et al. to modify the method of Lockhart et al. to include oligonucleotides comprising Alu sequences on

the array as extra calibrating probes. There would have been a reasonable expectation of success because Lockhart et al. and Chenchik et al. provide the details of procedures for making an array, preparing cDNA samples for hybridization, and making oligonucleotides comprising Alu sequence would have been known and routine skill in the art.

Therefore, the invention would have been obvious to a person of ordinary skill in the art at the time the invention was made.

20. Claims 1, and 6-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (WO 97/10365, 3/20/1997), as applied to claims 1, and 7-9 above, in view of Chenchik et al. (US patent no. 6,077,673, Date of Patent: June 20, 2000) and further in view of Feinberg et al. (Analytical Biochemistry, Vol. 132, pages 6-13, 1983).

The instant claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that either hybridize to a sufficient fraction of target molecules in a sample solution to which the array is exposed for hybridization (as required in claims 1-9), or hybridize to a majority of target molecules in the sample solution (as required in claims 10-14), and normalizing signals of features on the array using the calibrating probes by calculating a collective signal intensity. Claim 6 also requires that the calibrating probes are random sequence oligonucleotide.

As applied to claims 1, and 7-9, above, Lockhart et al. disclose a method of using oligonucleotide array for monitoring gene expression. The array is exposed to a sample solution containing cDNA molecules derived from the mRNA from a biological sample. The method comprises using an array containing not only oligonucleotide probes referred to as "test probes",

but also control probes used for calibration. The control probes include normalization controls, expression level controls such as probes from housekeeping genes, and mismatch controls. In one embodiment, Lockhart et al. teach that signals read from all other probes in the array are divided by the signals from the normalization control probes. See pages 34-35. Further, Lockhart et al. teach that the normalization of a signal can be accomplished by dividing the measured signal from the other probes in the array by the average signal produced by the normalization controls, and that normalization may also include correction for variations due to sample preparation and amplification. Such normalization may be accomplished by dividing the signal of a probe by the average signal from the sample preparation/amplification control probes (e.g. the Bio B probes). See page 54. It would have been readily recognized by one of skill in the art that when the average intensity from the control probes is calculated, a total intensity of the probes must have also been calculated. All the control probes disclosed by Lockhart et al. are interpreted as calibrating probes as in the instant claims because they are used to calibrate the signals of the test probes. The calibrating probes disclosed by Lockhart et al. will hybridize to a fraction of the target molecules in the sample solutions to which the array is exposed for hybridization because the housekeeping genes, etc. are contained in the sample solutions. Further, Lockhart et al. disclose a computer system to analyze the signal intensities detected from the array hybridization including computer readable medium on which data including signal intensities are stored and analyzed. See pages 55-56, and Figures 6-8.

However, Lockhart et al. do not explicitly recite that random sequence oligonucleotide are used as calibrating probes, and that the calibrating probes hybridize to a majority of the target molecules in the sample solution to which the array is exposed.

Chenchik et al. disclose a nucleic acid microarray and a process of using same for gene expression monitoring. The array is exposed to a sample solution containing cDNA molecules derived from the mRNA from a biological sample. In addition to the "probe spots", the array also comprises "calibration spots" and "control spots" (column 4, lines 12-20). Chenchik et al. indicate that the calibrating and control spots are to "provide other useful information, such as background or basal level of expression, and the like', and such spots "serve in the normalization of mRNA abundance and standardization of hybridization signal intensity in the sample assayed with the array" (column 8, lines 50-67 and column 9). While Chenchik et al. do not explicitly disclose using random sequence oligonucleotides as calibrating spots, they do motivate/suggest doing such by emphasizing that the calibrating probes should not be unique to a particular target in the sample, but "common" to the targets (column 8, lines 50-67).

A person of ordinary skill in the art would have been motivated by Chenchik et al. to search for probes that are common to the targets in the sample solution to modify Lockhart et al. to provide more calibrating probes for the microarray analysis.

Feinberg et al. teach a method of labeling a DNA by using a mixture of random hexamer as primers and state that the oligonucleotides bind to any DNA in high frequency. see page 6, abstract and pages 7-11). It would have been obvious to one of ordinary skill in the art that the random hexamer oligonucleotides would be ideal for a calibrating probe because it would meet the "common" standard proposed by Chenchik et al. One of ordinary skill in the art would have been motivated by Feinberg et al. and Chenchik et al. to modify the method of Lockhart et al. to include random hexamer oligonucleotides on the array as extra calibrating probes. There would have been a reasonable expectation of success because Lockhart et al. and Chenchik et al.

provide the details of procedures for making an array, preparing cDNA samples for hybridization, and making random hexamer oligonucleotides would have been known and routine skill in the art, and the random primers would have been actually commercially available.

Therefore, the invention would have been obvious to a person of ordinary skill in the art at the time the invention was made.

Conclusion

21. No claim is allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on 571-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

23. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the

problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shubo (Joe) Zhou, Ph.D.

Patent Examiner